ATTACHMENT B

REMARKS

By this amendment, Applicants have amended the claims in a manner which makes it clear that the claims are proper under the applicable USPTO guidelines concerning written description, and that the Examiner's rejection on the basis of this provision is without merit. In addition, other minor objections are also overcome without affecting the scope of the claims. As will be set forth below, under the applicable guidelines and legal principals, the present set of claims is clearly in compliance with Section 112, and in light of the fact that the present claimed antibody is clearly not disclosed or suggested in the prior art, the present application is in condition for immediate allowance.

In the Official Action, the Examiner rejected Claims 1-4 under 35 U.S.C. §102(b) as anticipated by the Hook et al. patent, US 5,648,240. In particular, although the Examiner recognized that the Hook '240 patent did not disclose or suggest the specific MAP10 protein of the present invention, much less antibodies that were capable of specifically binding with this protein, the Examiner argues that the '240 patent discloses isolated antibodies to the complete MAP protein which would inherently bind to the Map10 protein. In addition, the Examiner has stated that Applicants "are not asserting that the antibody of Hook et al. and [the present] antibody are different" and that "Applicants arguments are not that the antibodies of Hook are not capable of preventing infection and suitable for administration." However, contrary to the Examiner's assertions, and as Applicants have argued, it is indeed the case that the present antibody and the antibody disclosed in the Hook '240 patent are different, that the

antibody as disclosed in Hook would **not** "inherently bind" to the Map10 antigen of the present invention, and that the antibodies as disclosed in the Hook '240 patent have **not** been shown to be useful in treating infection, unlike the present antibodies which indeed give surprising and unexpected results in terms of treating infection. Accordingly, the present claimed antibody is different from the antibodies of the prior art and is not disclosed or suggested in the Hook reference.

Moreover, it is in fact the case that antibodies raised to a complete protein are normally quite different from antibodies raised against a very small and specific subregion of that protein for a variety of reasons. In particular, the complete protein usually has folds and other physical features which prevent many of the surface epitopes from generating antibodies at all, particularly if the particular site is only a small fraction of the entire protein. In addition, there may be other interference from blocking epitopes on other sites of the protein. As a result, it is more normally the case that an antibody directed to a specific subregion is patentable over an antibody generated against the whole protein, particularly when it can be shown that the antibody to the subregion has the ability to protect against infection in a manner not shown with the antibodies to the whole protein. See, e.g., U.S. Pat. No. 6,288,214 (Antibody to M55 subregion of the CNA protein patentable over prior art antibodies to the whole CNA protein).

The present case is a similar situation to the one in U.S. Pat. No. 6,288,214 In that the Map10 protein is a very small part of the entire MHC II analog protein, only about one-seventh of the size of the whole protein, and that the Map10 protein generates antibodies which are very different from those produced from the whole

protein. In particular, as reflected in the present specification, antibodies generated from the Map10 protein were capable of treating infection, and this is something which is not shown with regard to the antibodies in the Hook '240 patent. Accordingly, it is clear that the antibodies of the present invention are quite different that the antibodies disclosed in the Hook '240 patent, and contrary to the assertions of the Examiner, the present antibodies allow for treatment of infection in a manner not heretofore possible using the antibodies of the MHC II analog protein as disclosed in the Hook patent. It is thus the case that the present antibody is clearly not disclosed or suggested in the prior Hook patent and indeed gives significantly improved results with regard to treatment of infection in a manner not shown in the Hook patent. Accordingly, the present claims are clearly not disclosed or suggested in the Hook patent, and the Examiner's rejection on the basis of this reference is respectfully traversed and should be withdrawn.

In the Official Action, the Examiner rejected Claims 1-14, 18 and 23-28 under 35 U.S.C. §112 as failing to comply with the written description requirement. In addition to citing a number of cases which do not support the Examiner's position, the Examiner cites to the "Interim Written Description Guidelines" published June 15, 1998 in the Federal Register as supporting a rejection in this case. Unfortunately, the Examiner did not refer to the current "Revised Interim Written Description Guidelines" which are available on the USPTO's own web site, and which cover the present situation exactly and show that the Examiner's rejection is wholly without merit and contradicts the current guidelines with regards to antibodies.

In particular, a copy of the relevant pages from the current Written Description Guidelines (Example 16: Antibodies, pages 59-60, attached hereto as Appendix 1)

covers the present situation exactly, and indeed the present claim language is identical to the language of the version considered as adequate under the written description requirement. In short, the "Example specification" provided in the USPTO Guidelines discloses (1) the isolation of antigen X and that it is useful for a particular purpose such as detection of infection; (2) obtaining the purified antigen and provides a clear protocol by which the antigen was isolated and (3) "contemplates **but does not teach in an example antibodies which specifically bind to antigen X**" (emphasis added). Following the Example specification, the proposed claim is as follows:

"An isolated antibody capable of binding to antigen X"

In the Example specification, the conclusion, based on the level of skill and knowledge in the art of antibodies is that:

> "The disclosure **meets the requirements under 35 U.S.C. §112 first paragraph as providing an adequate written description of the claimed invention**" (emphasis added)

In the present case, Applicants specification discloses (1) the isolation of the Map10 antigen and that it is useful for a particular purpose such as detection of infection; (2) obtaining the purified antigen by providing a clear protocol by which the Map10 antigen was isolated and (3) **actually teaches several antibodies which were produced and which specifically bind to the Map10 protein**. In other words,

Applicants specification goes **beyond** the Example specification whish the US Patent Office Guidelines indicates satisfies the written description requirement, and actually discloses the production of the specific antibodies of the claims which would not have even been required to satisfy the Written Description requirement as per the guidelines. Accordingly, Applicants present Claim 1 which is directed to an isolated antibody capable of binding the Map10 antigen is **precisely** the type of claim that the Written Description Guidelines of the US Patent Office indicates has an adequate written description based on the specification. See also Enzo Biochem Inc. v. Gen-Probe Inc., 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002) (quoting the guidelines as showing that "the PTO would find compliance with § 112, for a claim to an 'isolated antibody capable of binding to antigen X'".)

Accordingly, the Examiner's rejection on the basis of the written description requirement under 35 U.S.C. §112 is respectfully traversed and should be withdrawn as totally opposite to the law and the Patent Office's own Written Description Guidelines.

In the Official Action, the Examiner rejected Claims 1-14, 18 and 23-28 under 35 U.S.C. §112 as failing to comply with the enablement requirement. In short, the Examiner argues that it would take undue or "extensive" experimentation to make and use the present invention. However, in light of the fact that one skilled in the art would not have any problems in making and using the present invention, particularly in light of the USPTO's comments in the Written Description Requirement above regarding the state of knowledge when it comes to antibodies, and in light of the decision in "In re Wands" discussed below, it is clear that there is no grounds for a rejection on the basis

of "undue experimentation", and that the Examiner's rejection is without merit and should be withdrawn.

In the first place, as indicated in the attached Appendix 1, the Patent Office states that with regard to the skill in the art concerning antibodies:

> "The level and skill in the art of antibodies at the time of filing was such that production of antibodies against a well-characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.
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> * * *
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> "Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X."

Clearly, in light of the Patent Office's **own guidelines** regarding the **level of skill in the antibody art**, it is clearly improper for the Examiner to argue that one of ordinary skill in this art could not make or use the present invention which is simply an antibody capable of binding to Map10. The Examiner's assertions regarding modifications to proteins is somewhat irrelevant since in the first place, the skilled artisan will clearly be able to make and use the present invention, i.e., produce the claimed antibodies from the well known and well defined Map10 antigen, and secondly, no matter what

modifications are made to proteins, the bottom line is that the determination of whether a particular antibody is capable of binding to Map10 is well within the routine skill of the ordinary artisan, and thus does not present any "undue experimentation" problems for the skilled artisan.

Moreover, with regard to whether there is "undue experimentation" present so as to support a rejection under the enablement provision of Section 112, the one case which is the standard by which an enablement rejection must be assessed is the Federal Circuit decision of In re Wands which established the criteria for a determination of whether a claim in objectionable on the basis of undue experimentation. It is not surprising that the Examiner **did not** refer to the Wands case in the Official Action, since if the Examiner had referred to this case, it would have shown that this is simply **not** a case of "undue experimentation" as defined in Wands. In particular, the case of in re Wands, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) was a case dealing with monoclonal antibodies used in an immunoassay, and the original Examiner and the Patent Board of Appeals had claimed there was "undue experimentation" because some screening was necessary to obtain the high-binding monoclonal antibodies in accordance with the claims. In the examples disclosed in the specification, out of an original 143 hybridomas prepared in accordance with the invention, only 9 were deemed suitable for further analysis, and only 4 of these were shown to have the high binding affinity needed for the antibodies of the claims.

However, despite the fact that multiple experiments were necessary to obtain antibodies which met the requirements of the claims, and despite the fact that the experiments led to many attempts which did not result in the claimed antibodies, the

Federal Circuit **reversed** the Examiner and the Board and held that the claims were in fact enabled because there was reasonable guidance provided in the application, and because any necessary experimentation was simply **routine** one of ordinary skill in the art. In particular, the Federal Circuit held that the test for "undue experimentation" was not merely quantitative, but instead was based on whether any experimentation needed was **routine**. As the Court stated, "the test is not merely quantitative, since a considerable amount of experimentation is permitted, **if it merely routine**, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." 8 U.S.P.Q.2d at 1404 (emphasis added). Accordingly, the Federal Circuit held that there was **no** "undue experimentation" necessary to make and use the invention because the Applicants had provided "considerable direction and guidance on how to practice their invention and provided working examples" and because practitioners in this art were well prepared to screen hybridomas in order to find one that made the desired antibody. 8 U.S.P.Q.2d at 1406.

In the present case, Applicants provide specific guidance that is well sufficient for one skilled in the art to make and use the invention which is an isolated antibody which is capable of binding to the Map10 protein from *Staphylococcus aureus*. In order to make and use the present invention, one needs merely to raise antibodies to Map10 and then screen the generated antibodies to determine if they bind to Map10. It is abundantly clear that such techniques are well within the capability of the ordinary practitioner in the art and will require at most routine screening using methods well known in the art. Moreover, the US Patent Office has recognized that techniques of

producing and screening antibodies are well known and routine in the art, as reflected in the Written Description Guidelines (see Appendix 1) which state:

> "The level and skill in the art of antibodies at the time of filing was such that production of antibodies against a well-characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.
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> * * *
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> "Considering the **routine** art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X." (emphasis added.)

Since the US Patent Office has recognized that it is **routine** and well within the skill of the ordinary artisan to produce antibodies from a known antigen, the established criteria of the Wands case precludes a rejection on the basis of undue experimentation since where "routine" experimentation is all that is necessary, the experimentation cannot be considered "undue". Accordingly, the Examiner's rejection under 35 U.S.C. §112 on the basis of "undue experimentation" is improper and should be withdrawn.

The last remaining objection was on the basis that "acronyms such as Map10 and S. aureus" should be spelled out when first introduced in the claims. With regard to "S. aureus", Applicants have now spelled out this term in the first claim so as to obviate the rejection. However, "Map10" is not an acronym, but instead is the name the inventors gave to this protein, and this term is now accepted as the name for this protein as would be well understood by one skilled In the art. Accordingly, the use of "Map10" is proper in this case since it is not an acronym for anything else, and thus the claims using this term are entirely proper under 35 U.S.C. § 112.

In light of the amendments and arguments as set forth above, Applicants submit that the present application overcomes all prior rejections and has been placed in condition for allowance. Such action is earnestly solicited.

END OF REMARKS

APPENDIX 1

Example 16: Antibodies

Specification: The specification teaches that antigen X has been isolated and is useful for detection of HIV infections. The specification teaches antigen X as purified by gel filtration and provides characterization of the antigen as having a molecular weight of 55 KD. The specification also provides a clear protocol by which antigen X was isolated. The specification contemplates but does not teach in an example antibodies which specifically bind to antigen X and asserts that these antibodies can be used in immunoassays to detect HIV. The general knowledge in the art is such that antibodies are structurally well characterized. It is well known that all mammals produce antibodies and they exist in five isotypes, IgM, IgG, IgD, IgA and IgE. Antibodies contain an effector portion which is the constant region and a variable region that contains the antigen binding sites in the form of complementarity determining regions and the framework regions. The sequences of constant regions as well as the variable regions subgroups (framework regions) from a variety of species are known and published in the art. It is also well known that antibodies can be made against virtually any protein.

Claim: An isolated antibody capable of binding to antigen X.

Analysis:

A review of the full content of the specification indicates that antibodies which bind to antigen X are essential to the operation of the claimed invention. The level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against a well-

characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.

The claim is directed to any antibody which is capable of binding to antigen X.

A search of the prior art indicates that antigen X is novel and unobvious.

Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

Conclusion: The disclosure meets the requirement under 35 USC 112 first paragraph as providing an adequate written description of the claimed invention.